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Mass Spectrometric Fragmentation of the Tautomers of 1,3-Diketones

A Gas Chromatographic/Mass Spectrometric Study

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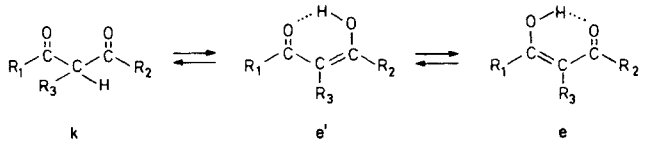
The diketo and ketoenol tautomers of aliphatic 1,3-diketones can be easily separated by gas chromatography. The mass spectra of tautomers of pentane-2,4-diones substituted at C(1) and C(3), separated in this way, have been obtained. The fragmentation mechanisms are discussed. The mass spectra of the tautomers are quite different, and the main fragmentation pathways can be easily linked to the structures of the (non-interconverting!) tautomeric molecular ions. Furthermore, isomers differing by the position of the substituent can also be identified by their mass spectra.

INTRODUCTION

1,3-Diketones are very important intermediates in organic synthesis. Accordingly, the electron impact (EI) mass spectra and the mass spectrometric fragmentations of these compounds have been thoroughly studied.[1] However, 1,3-diketones are characteristically an equilibrium mixture of tautomers, i.e. of the diketone **k** and the corresponding ketoenols **e** and **e'** (Scheme 1). The



Scheme 1

equilibrium depends on the details of the structure of the 1,3-diketone and on the experimental conditions; the composition of the tautomer mixture in the gas phase is usually not known. Hence, the EI mass spectra of 1,3-diketones obtained with a heated batch inlet system correspond to those of an unknown mixture of tautomeric compounds, and it can be shown only by indirect methods which fragment ions arise from which tautomer.[2] This implies that the molecular ions of these tautomers should exist as stable species without rapid interconversion and fragment by separate reaction channels.

During a study of rearrangement reactions of the molecular ions of 1,3-diketones,[3] we noticed that the tautomers **k** and **e** or **e'**, respectively, can be separated by gas chromatography (GC) and investigated by GC/MS. This makes it possible to measure the EI mass spectra of the pure tautomers of 1,3-diketones directly and is of interest both for the analytical application of mass spectrometry to this important class of compounds and for the study of the fragmentation mechanisms of 1,3-diketone ions.

RESULTS AND DISCUSSION

The 1,3-diketones investigated in this study are given in Table 1. These compounds are derived from pentane-2,4-dione (**1**) by substitution at C(1) and/or C(3). Also indicated in Table 1 is the composition of the tautomeric mixture as determined by GC/MS, assuming the same ionization cross-section of the tautomers **k** and **e**. The 3,3-disubstituted derivatives **15** and **16** exist only in the diketo form **k**. Only the enolic tautomers **e** are observed for the 1-monosubstituted pentane-2,4-diones **7**, **8** and **11**, while diketone **k** and ketoenol **e** are found in all other cases.

It is known that the tautomerization of ketones and enols in solution is a bimolecular reaction which involves protonated diketones or enolate ions as intermediates and which is catalysed by acids or bases.[4] In the gas phase and in the neutral liquid phase of a gas chromatograph, the keto-enol interconversion is slow and the tautomers are eventually separated. In the case of all 1,3-diketones investigated, only one ketoenol tautomer has been observed, in spite of the two possible structures **e** and **e'**. The interconversion of the tautomers **e** and **e'** probably occurs by a fast intramolecular reaction. The *E* and *Z* isomers of **e** have been separated during GC in favourable cases, though.

In agreement with a slow diketone-ketoenol interconversion, one observes the fast incorporation of just one D atom into each of the separated tautomers, if 1,3-diketone and D_2O are co-injected into the gas chromatograph. The exchange of all acidic H atoms (bound to O or C) is complete within a few minutes, however, if the

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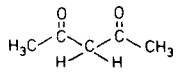
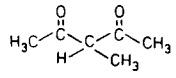
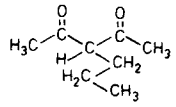
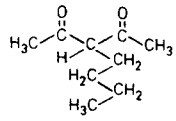
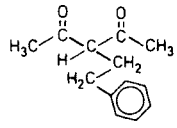
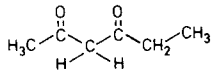
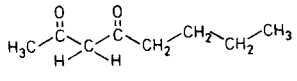
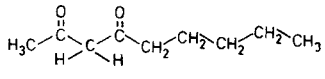
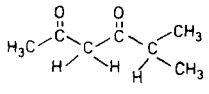
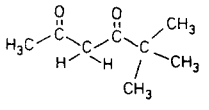
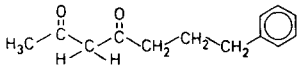
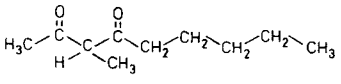
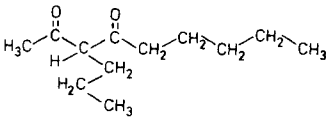
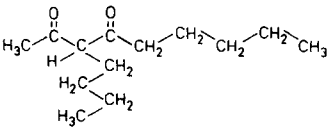
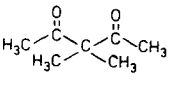
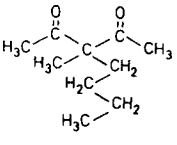
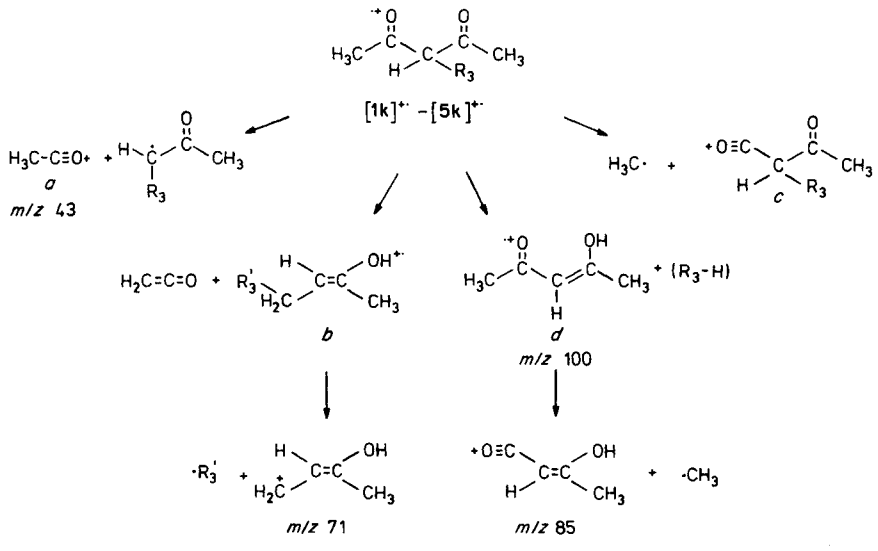
Table 1. List of 1,3-diketones investigated

Compound	No.	Tautomeric composition[a] (%)		Retention index
	1	k e	4 96	818 794
	2	k e	63 37	884 984
	3	k e	77 23	1024 1104
	4	k e	81 19	1158 1198
	5	k e	71 29	1605 1681
	6	k e	0.5 99.5	936 891
	7	k e	0 100	 1093
	8	k e	0 100	 1188
	9	k e	1 99	961 947
	10	k e	1 99	1010 993
	11	k e	0 100	— 1703
	12	k e	70 30	1273 1355
	13	k e	81 19	1404 1475
	14	k e	81 19	1497 1570
	15	k	100	920
	16	k	100	1201

[a] Determined by GC after injection of a 1% ether solution.



Scheme 2

diketone and D_2O are injected into a heated batch inlet system.[5] It is assumed that the H-D exchange of the hydroxy group of **e** is fast in spite of the internal hydrogen bond, and the fast D incorporation has been used for the identification of the ketoenol tautomers **e**. This assignment agrees with a rationalization of the fragmentations of the tautomeric molecular ions (see below).

The 70 eV mass spectra of the tautomers of a 1,3-diketone differ greatly. Interestingly, this also proves that the molecular ions of the tautomers of a 1,3-diketone do not interconvert within the residence time in the ion source. Hence, these 1,3-diketones add further examples to the list of tautomeric ions which do not tautomerize prior to decomposition in the ion source of a mass spectrometer.[6] A detailed study of metastable molecular ions of the tautomers of 1,3-diketones reveals that even at the rather long reaction times no isomerization by a 1,3-hydrogen shift is observed, but H atom transfers by 1,4- and 1,5-shifts do occur if possible. The main reactions observed in the mass spectra of the 1,3-diketones **1–16** are fragmentations by McLafferty rearrangements and by allylic cleavages as noted before.[1] For clarity, the 1,3-diketones corresponding to different types of substitution of pentane-2,4-dione (**1**) are discussed separately.

3-Substituted pentane-2,4-diones, 1–5

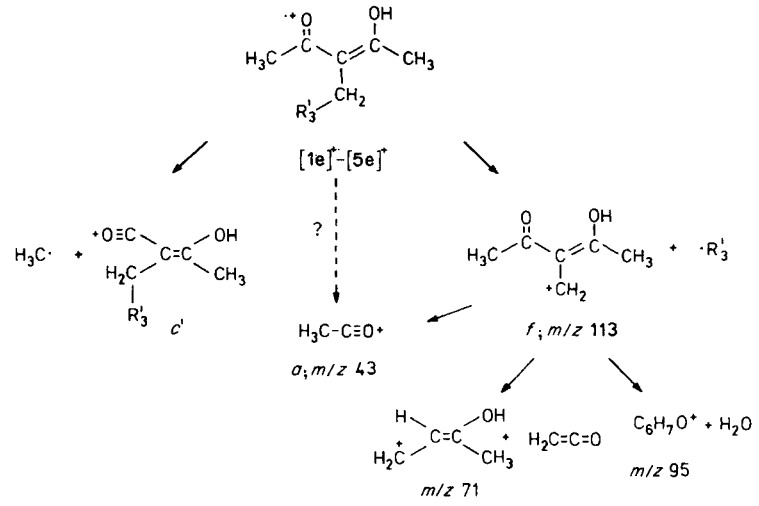
The mass spectrometric fragmentations of the diketo form **k** of **1–5** are summarized in Scheme 2, and the relative intensities of the characteristic ion peaks in their 70 eV EI mass spectra are given in Table 2. The intensities of the molecular ions peaks are rather small and, with the exception of **5**, the base peak is formed by the acetylium ion $[CH_3CO]^+$ (*a*) at *m/z* 43, which can arise from α-cleavages at either keto group. The loss of a (terminal) methyl group, which would also correspond to an α-cleavage, is observed only with low intensity. The other two primary fragmentations of the molecular ions $[\mathbf{1k}]^{+\cdot}$–$[\mathbf{5k}]^{+\cdot}$ are McLafferty rearrangements. The first one corresponds to elimination of ketene and gives rise to enol ion *b*, which fragments by allylic loss of the substituent R_3. The second McLafferty rearrangement eliminates the substituent R_3 as an alkene molecule and forms the ketoenol ion *c* of pentane-2,4-dione, *m/z* 100. In agreement with Stevenson's rule,[7] the charge remains at the alkene fragment if its ionization energy (*IE*) is lower than that of the ketoenol tautomer of pentane-2,4-dione. Obviously, this is the case for the β-phenylethyl-substituted derivative **5k**, which forms a styrene ion, *m/z* 104, by this rearrangement to give the base peak in its mass spectrum. Hence, styrene (*IE* = 8.47 eV)[8] accepts the positive charge, and this indicates that the literature value of *IE* = 8.87 eV[8] for pentane-2,4-dione corresponds very probably to the *IE* of the ketoenol tautomer (see below for *IE* of diendiol tautomers). Ion *d* fragments further by loss of CH_3 via an allylic α-cleavage and not by loss of ketene, that is, its reactions agree with those of the molecular ions of the ketoenol tautomer **1e** and not with those of the diketo form **1k**. Thus, again, no fast tautomerization $[\mathbf{1e}]^{+\cdot} \rightleftarrows [\mathbf{1k}]^{+\cdot}$ via a 1,3-hydrogen shift is observed in ions *d*.

The mass spectrometric fragmentations of the ketoenol tautomers **1e–5e** are shown in Scheme 3, and the relative intensities of the relevant ion peaks are given in Table 3. The intensities of the molecular ions of these ketoenol tautomers are distinctly larger than those of the diketo counterparts. The base peak, again with the exception of **5e**, is still given by the acetylium ion *a*, but this ion arises probably not directly from the

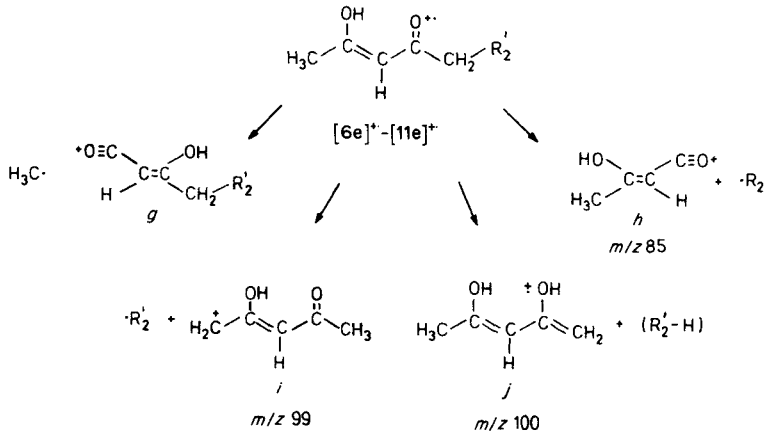
Table 2. Relative intensities of the ion peaks in the 70 eV mass spectra of the ketones 1k–5k

	$M^{+\cdot}$	*a*	*b*	*c*	*d*
1k	6	100	4	2	6[a]
2k	2	100	24	5	—
3k	0.5	100	31	—	31
4k	0.5	100	5	—	11
5k	0.5	52	—	—	100[b]

[a] Identical mass to the molecular ion.
[b] *m/z* 104 because of reverse charge distribution.



Scheme 3



Scheme 4

molecular ions, which could require the cleavage of a vinylic C—C bond. The preferred fragmentations of the molecular ions $[\mathbf{1e}]^{+\cdot}$-$[\mathbf{5e}]^{+\cdot}$ are two allylic cleavages. The first gives rise to loss of a terminal methyl group, while the second occurs via cleavage of a C—C bond in the substituent R_3 to form ion *f*. As is usual for competing cleavages, the loss of the larger and more stable alkyl radical is preferred. Hence, loss of a stable benzyl radical from $[\mathbf{5e}]^{+\cdot}$ by this reaction gives rise to the base peak at *m/z* 113. Hydrogen migrations are also clearly involved in the further fragmentations of ion *f* by losses of ketene and H_2O.

Table 3. Relative intensities of the ion peaks in the 70 eV mass spectra of the enol 1e–5e

	$M^{+\cdot}$	*a*	*c'*	*f*
1e	31	100	50	—
2e	39	100	57	0
3e	16	100	9	71
4e	5	100	3	41
5e	2	65	0.5	100

1-Substituted pentane-2,4-diones, 6–11

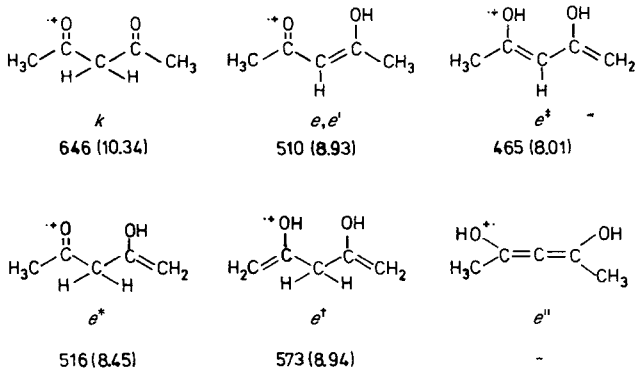
The ketoenol tautomers **6e–11e** are the main components in the mixtures of tautomers, and their characteristic mass spectrometric fragmentations are summarized in Scheme 4 and Table 4. In contrast with their 3-substituted analogues, the primary fragmentations of the molecular ions $[\mathbf{6e}]^{+\cdot}$-$[\mathbf{11e}]^{+\cdot}$ correspond to α-cleavages/allylic cleavages *and* to a McLafferty rearrangement.

Table 4. Relative intensities of the ion peaks in the 70 eV mass spectra of enols 6e–11e

	$M^{+\cdot}$	*g*	*h*	*i*	*j*
6e	39	21[a]	100	21[a]	—
7e	5	7	100	1	41
8e	2	4	100	8	38
9e	29	3	100	—	—
10e	38	3	100	(8)[b]	—
11e	3	0	98	0	100

[a] Identical mass for ions *i* and *g*.
[b] Another ion structure such as *i*.

Depending on the structure **e** and **e'** of the tautomer, α-cleavage/allylic cleavage adjacent to the carbonyl group gives rise to a methyl radical and ion *h*. The ions *h* predominate in the 70 eV mass spectra (base peak for **6e–10e**), and this means either that the tautomeric ion of **e** is formed in large excess or the loss of the larger alkyl radical is preferred, as usual, from a mixture of equilibrating ions of **e** and **e'**. The latter explanation is probably correct because, in all mass spectra of **6e–10e**, one observes an ion *i* with moderate abundance at *m/z* 99, which arises from loss of the substituent at C(1) via an allylic cleavage in ions of structure **e**. In the case of **11e**, this also explains the formation of $[C_7H_7]^+$ ions by a reverse charge distribution. Ions *j* are formed with large relative abundances by loss of the substituent at C(1) as an alkene molecule via a McLafferty rearrangement (base peak for **11e**). This fragmentation differentiates between the 3- and 1-substituted pentane-2,4-diones, and its absence in the case of **[2e]**$^{+\cdot}$-**[5e]**$^{+\cdot}$ clearly shows that a tautomeric ion *e''* (Scheme 5) with cumulated double bonds is not formed because of its large



Scheme 5

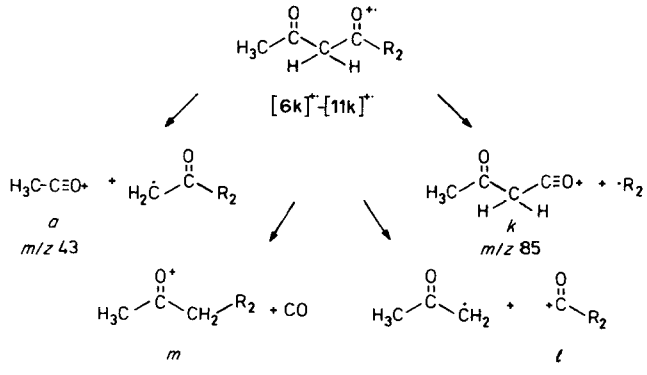
heat of formation. In contrast to the elimination of the substituent at C(3), the elimination of the substituent at C(1) via a McLafferty rearrangement gives rise to a tautomeric ion $e^{\ddagger}$ with conjugated double bonds (Scheme 5). MNDO calculations of the heat of formation of ions *k*, *e*, *e**, $e^{\dagger}$, *e''* and $e^{\ddagger}$ show[9] that the dienediol $e^{\ddagger}$ is the most stable tautomeric molecular ion of 1,3-diketones (Scheme 5). In this respect, it is significant that during this McLafferty rearrangement of **11e**, which forms a dienediol fragment and a styrene fragment, the positive charge can be carried by each of these fragments (ions *m/z* 100 and 104, respectively). Thus, *IE*(dienediol $e^{\ddagger}$) should be smaller than *IE*(styrene) = 8.47 eV, in agreement with the calculated value of 8.01 eV.

Although the diketo forms **6k–11k** are only very minor components in the mixture of the tautomers, their EI mass spectra can be obtained by GC/MS in **6k**, **9k** and **10k** (Scheme 6). The main fragmentations of these molecular ions involve the formation of ions *m/z* 85 by α-cleavage and formation of the acetylium ion *m/z* 43 and the other possible acylium ion *l*, probably also by α-cleavage. In **10k**, the charge may remain with the tertiary C_4H_9 fragment to give ions *m/z* 57. Interestingly, and in contrast with the mass spectra of the other diketo tautomers, the mass spectra of **6k**, **9k** and **10k** exhibit an intense peak for the loss of CO. The mechanism of

Table 5. Relative intensities of the ion peaks in the 70 eV mass spectra of ketones 6k, 9k and 10k

	$M^{+\cdot}$	*a*	*k*	*l*	*m*
6k	24	100	28	41	11
9k	21	100	44	16	10
10k	15	70	59[a]	59[a]	36

[a] Identical mass for ions *k* and *l*.



Scheme 6

this interesting fragmentation will be dealt with in a forthcoming paper.[10]

1,3-Disubstituted pentane-2,4-diones, 12–14, and 3,3-disubstituted pentane-2,4-diones, 15 and 16

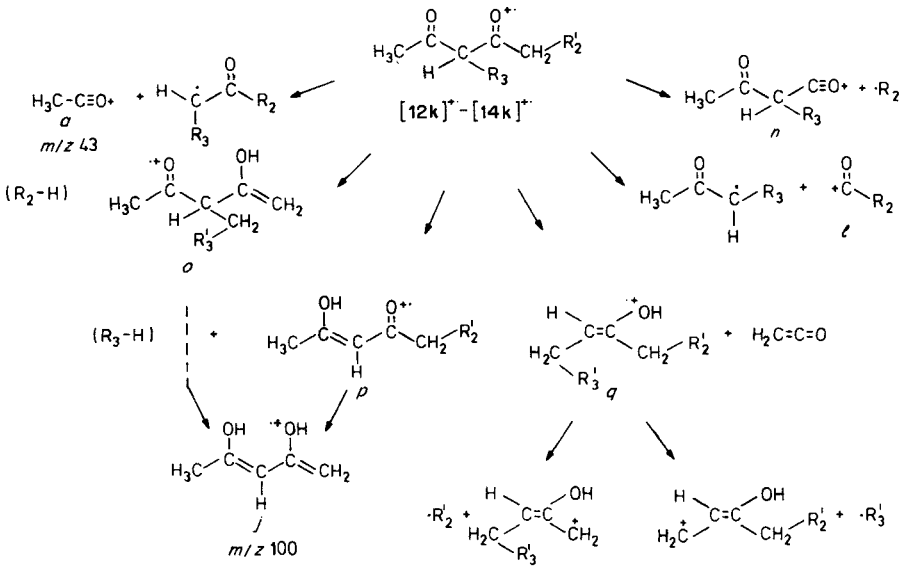
The fragmentations of the diketo forms of **12k–14k** are summarized in Scheme 7, and the corresponding ion peak intensities are given in Table 6. With the information concerning the mass spectrometric fragmentations of the monosubstituted pentane-2,4-diones, the reactions of the molecular ions **[12k]**$^{+\cdot}$-**[14k]**$^{+\cdot}$ are easy to understand. The abundances of these molecular ions in the 70 eV mass spectra are small, as in the case of the other diketo tautomers **1k–5k**, and the base peak is formed by the acetylium ion *m/z* 43. The primary fragmentation of the molecular ions corresponds to α-cleavages with preferred loss of the larger radical and to loss of ketene and alkene molecules from the substituents at C(1) and C(3) via McLafferty rearrangements.

The relative abundances of the McLafferty product ions are small because of facile fragmentations by either a second McLafferty rearrangement or an allylic cleavage. Hence, the peaks in the mass spectra of **12k–14k** are easily rationalized by the fragmentations given

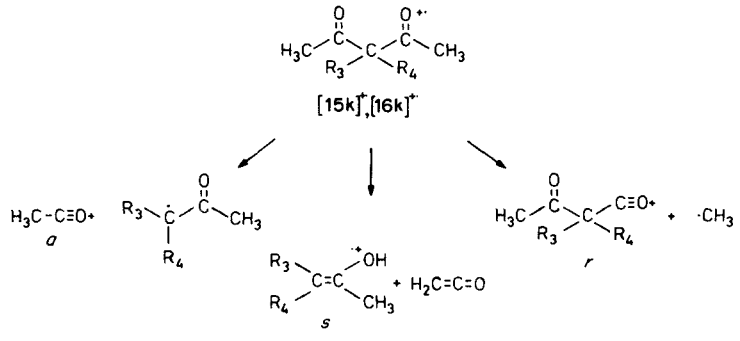
Table 6. Relative intensities of the ion peaks in the 70 eV mass spectra of ketones 12k–14k

	$M^{+\cdot}$	*a*	*j*	*l*	*n*	*o*	*p*	*q*
12k	1	100	—	42[a]	42[a]	2	—	0.5
13k	1	100	26	41	6	0.5	4	4
14k	1	100	11	44	2	3	3	0.5

[a] Identical mass for ions *l* and *n*.



Scheme 7



Scheme 8

in Scheme 7, but, because of the multiple fragmentation pathways leading to most fragment ions, it is not possible to assign structures and modes of generation without further experimental information. This is also the case for the mass spectrometric fragmentations of the 3,3-disubstituted pentane-2,4-diones **15k** and **16k**. The relevant fragmentation pathways are shown in Scheme 8, and the corresponding ion peak intensities are given in Table 7. The peaks of the molecular ions could not be detected in the 70 eV mass spectra obtained by GC/MS, and the ions observed with the highest mass correspond to the production of the ketene loss or alkene loss by a McLafferty rearrangement. These ions have the structure of enol ions, and as in the case of other **e**-type tautomers, further fragmentation occurs easily by allylic bond cleavages within the substituents at C(3).

Scheme 9 and Table 8 present the characteristic data for the 70 eV mass spectra of the ketoenol tautomers **12e–14e**. In contrast with the **k** tautomers, the mass spectra show distinct peaks for the molecular ions. The decomposition of the molecular ions is dominated by α-cleavages/allylic cleavages as discussed for the C(1)- and C(3)-monosubstituted compounds. The two possible acylium ions $[CH_3CO]^+$ and $[R_1CH_2CO]^+$, arising at least formally from α-cleavages, are also observed with large abundances. However, there is also a fragmentation pathway involving an alkene elimination from R_1 via a McLafferty rearrangement, but no alkene loss is observed from R_3. This agrees again with the reactions of monosubstituted **e**-type tautomers and allows an easy differentiation between substituents attached at C(1) or C(3) in pentane-2,4-diones.

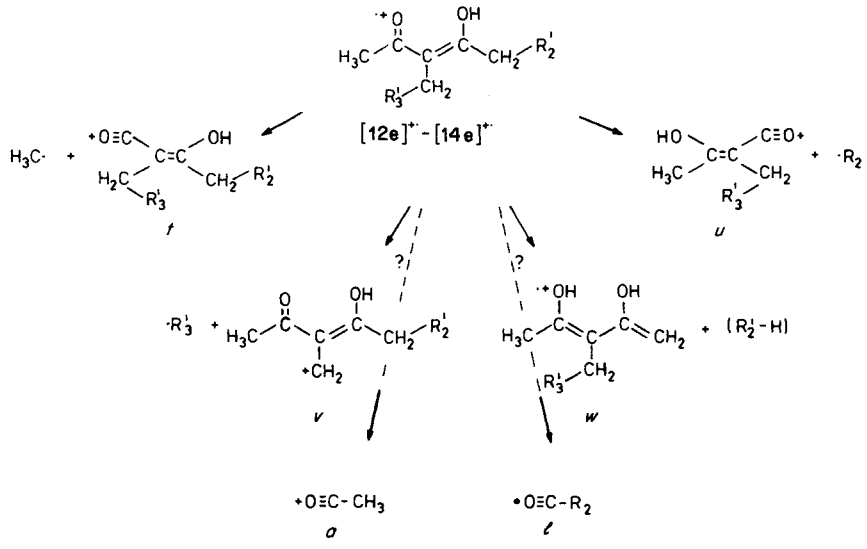
Table 7. Relative intensities of the ion peaks in the 70 eV mass spectra of ketones 15 and 16

	$M^{+\cdot}$	*a*	*s*	*r*
15k	0.2	100	36	0.4
16k	0	78	35	0

Table 8. Relative intensities of the ion peaks in the 70 eV mass spectra of enols 12e–14e

	$M^{+\cdot}$	*a*	*l*	*t*	*u*	*v*	*w*
12e	10	63	100[a]	6	100[a]	—	19
13e	10	100	53	6	76	20	7
14e	5	100	71	4	51	24	4

[a] Identical mass for ions *l* and *u*.



Scheme 9

CONCLUSION

The fragmentations deduced from the 70 eV EI mass spectra of separated tautomers **k** and **e** of pentane-2,4-dione and its C(1)- and C(3)-substituted derivatives (see Schemes 1–8) fully conform the reactions which have been proposed by the mass spectrometric investigation of neat samples of these compounds.[1,2] However, the present results give a much clearer picture of the fragmentation reactions of the tautomeric molecular ions. It is shown that the molecular ions of the tautomers **k** and **e** of the 1,3-diketones are distinct stable species in the gas phase and do not tautomerize prior to decomposition in the ion source. The primary fragmentation reactions of these ions are quite different from each other.

The intensities of the molecular ion peaks of the diketo tautomers **k** are small and decompositions by McLafferty rearrangements are favoured. This can be attributed to the presence of the two carbonyl groups as acceptors for the H atom during the first step of this reaction. A ketene and an alkene molecule originating from alkyl groups at C(1) and C(3), respectively, can be lost by these reactions. The peaks of the molecular ions of 3,3-dialkylpentane-2,4-diones have not been detected in the mass spectra, and elimination of a C(3) substituent via McLafferty rearrangement gives rise to ions with the structure of the ketoenol tautomers **e** of the C(3)-monoalkylated derivatives. Hence, the EI mass spectra of neat samples of C(3)-mono- and dialkylated pentane-2,4-diones are similar, and EI mass spectrometry is not very useful in detecting the presence of small amounts of the dialkylated product in 3-alkylpentane-2,4-diones without gas chromatographic separation.

The mass spectra of the ketoenol tautomers **e** clearly show the peaks of the molecular ions, which can be attributed to the greater stability of enol ions over keto ions. The preferred fragmentations of these ions of **e** are loss of alkyl radicals by α-cleavages and/or allylic cleavages. In contrast with the tautomeric ions of **k**, no loss of ketene is observed. Furthermore, only alkyl substituents at C(1) (or C(5)), but not at C(3), are lost as alkene molecules by a McLafferty rearrangement.

The differences in the mass spectrometric behaviour of the tautomeric ions of **e** and **k** of pentane-2,4-dione derivatives and the predominant fragmentation reactions of these ions are clearly linked to the structures of the tautomers. In fact, these tautomers provide textbook examples for the correlation between structures and EI mass spectra of organic compounds. The type and the position of substituents at C(1) and/or C(3) of the pentane-2,4-diones can be easily derived from the EI mass spectra, especially in the case of the ketoenol tautomers **e**. Thus, GC/MS also proves to be a very valuable tool for the structure analysis of 1,3-diketones.

EXPERIMENTAL

The GC/MS spectra of the 1,3-diketones were measured with a quadrupole mass spectrometer Finnigan MAT 1020 B. The electron energy was 70 eV. The keto-enol tautomers were separated by GC using a capillary column of type SE 54, chemical bonded (i.d. 0.25 mm, film thickness 0.25 μm, length 30 m) and the following GC conditions: zone temperature, 250 °C; initial temperature, 60 °C; initial time, 3 min; ramp rate, 15 °C min^{-1}; final temperature, 250 °C (for 30 min.).

Labelling experiments were used to correlate the GC peaks with one of the corresponding tautomers. It is well known,[5] that the H–D exchange proceeds much faster with OH than with acidic CH groups. This can be observed by a mass shift in the spectra. So, rinsing the GC column with D_2O, H–D exchange occurs only in the enol tautomer during the separation process and can be used to identify this tautomer.

Pentane-2,4-dione is commercially available from Aldrich Chemical Co. The C(3)-substituted pentane-2,4-diones **2–5** and **12–16** were prepared following the syntheses of **2** described by Chong and Clezy.[11] The 1,3-

diketones **6–8** and **11** were obtained by alkylation of pentane-2,4-dione with $NaNH_2$ in liquid NH_3.[12] Compounds **9** and **10** were synthesized by a Claisen condensation of the appropriate ketone and ethyl acetate described by Adams and Hauser.[13]

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